Herbicides

General Information

Herbicides are used to control broadleaf weeds and woody plants on agricultural and residential property. These chemicals can be classified as chlorophenoxy acids (e.g., 2,4,5-trichlorophenoxyacetic acid, 2,4-dichlorophenoxyacetic acid), triazines (e.g,. atrazine), and chloroacetamides (e.g., alachlor). The U.S. EPA has restricted use of all these chemicals. Concern about contamination of 2,4,5-trichlorophenoxyacetic acid with 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) has led to the discontinuation of this herbicide. The general population may be exposed to this and other herbicides from their residential use, by living near application sites, or by ingesting herbicide-contaminated food or water. Workers who manufacture, formulate, or apply these chemicals also may be exposed to them. The FDA, U.S. EPA, and OSHA have developed criteria for the allowable levels of these chemicals in foods, the environment, and the workplace.

Atrazine is a commonly used herbicide in this country. Atrazine is listed as a "not classifiable" human carcinogen by IARC and as "not a likely human carcinogen" by U.S. EPA. 2,4-dichlorophenoxyacetic acid (2,4-D) is also used in the United States and is listed as a possible human carcinogen by IARC.

Table 177 shows the various metabolites and their parent herbicides. For example, atrazine is metabolized to atrazine mercapturate. The presence of these chemicals in a person generally reflects recent exposure to herbicides. In addition to reflecting exposure to the parent herbicide, the level of the metabolite in a person's blood or urine may also reflect exposure to the metabolite itself if it was present in the person's environment.

Interpreting Urine Herbicide Levels Reported in the Tables

Generally recognized guidelines for urine levels of these metabolites have not been established. Urine levels of the herbicides were measured in a subsample of NHANES 1999-2000 participants aged 6-59 years. Subsamples were randomly selected within the specified age range to be a representative sample of the U.S. population. Measuring these chemicals at these levels is possible because of advances in analytical chemistry. Finding a measurable amount of one or more herbicide in the urine does not mean that the levels of the herbicides cause an adverse health effect. Whether herbicides at the levels reported here are cause for health concern is not known; more research is needed.

These data provide physicians with a reference range so that they can determine whether people have been exposed to higher levels of herbicides than those found in the general population. Tables 178-187 summarize the results of these measurements. These data will help scientists plan and conduct research on exposure to organochlorines and their health effects.

Table 177. Herbicides and their metabolites

Herbicide (CAS number)	**Urinary metabolite** (CAS number)
Salts and esters of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) (93-76-5)	2,4,5-Trichlorophenoxyacetic acid (93-76-5)
Salts and esters of 2,4-dichlorophenoxyacetic acid (2,4-D) (94-75-7)	2,4-Dichlorophenoxyacetic acid (94-75-7) 2,4-Dichlorophenol (minor) (120-83-2)
Alachlor (15972-60-8)	Alachlor mercapturate
Atrazine (1912-24-9)	Atrazine mercapturate

2,4,5-Trichlorophenoxyacetic acid

CAS No. 93-76-5

Ninety percent of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) is eliminated unchanged in human urine. The route of worker exposure to 2,4,5-T is dermal, although inhalation can occur, depending on the method of application. Applicators had urine 2,4,5-T levels ranging from 250 µg/L to 11,000 µg/L (Simpson et al., 1978; Kolmodin-Hedman et al., 1980). Only 1.2% of participants in the NHANES 1999-2000 subsample had detectable levels of this chemical.

Table 178. 2,4,5-Trichlorophenoxyacetic acid

Geometric mean and selected percentiles of urine concentrations (in µg/L) for the U.S. population aged 6 to 59 years, National Health and Nutrition Examination Survey, 1999-2000.

	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)						Sample size
		10th	25th	50th	75th	90th	95th	
Total, age 6-59	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	1814
Age group								
6-11 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	430
12-19 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	618
20-59 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	766
Gender								
Males	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	891
Females	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	923
Race/ethnicity								
Mexican Americans	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	652
Non-Hispanic blacks	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	483
Non-Hispanic whites	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	530

< LOD means less than the limit of detection, which averaged 0.14 µg/L (SD 0.35, maximum value 1.20).

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

Table 179. 2,4,5-Trichlorophenoxyacetic acid (creatinine adjusted)

Geometric mean and selected percentiles of urine concentrations (in µg/gram of creatinine) for the U.S. population aged 6 to 59 years, National Health and Nutrition Examination Survey, 1999-2000.

	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)						Sample size
		10th	25th	50th	75th	90th	95th	
Total, age 6-59	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	1814
Age group								
6-11 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	430
12-19 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	618
20-59 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	766
Gender								
Males	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	891
Females	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	923
Race/ethnicity								
Mexican Americans	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	652
Non-Hispanic blacks	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	483
Non-Hispanic whites	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	530

< LOD means less than the limit of detection (see previous table).

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

2,4-Dichlorophenoxyacetic acid

CAS No. 94-75-7

About 95% of absorbed 2,4-dichlorophenoxyacetic acid (2,4-D) is excreted in the urine, mostly as unchanged 2,4-D. The 90th percentile for adults in a non-random subsample from NHANES III (1988-1994) (Hill et al., 1995) was 1.2 µg/gram of creatinine. Levels in children reported here are similar to levels in children from a reference community in Arkansas (Hill et al., 1989) who were studied in 1988-1994. Levels of 2,4-D were found to increase threefold to tenfold over pre-application levels when measured in 2,4-D spray applicators (Draper et al., 1982). Levels reaching 30 mg/L (30,000 µg/L) have been reported in herbicide workers (Lauwerys and Hoet, 2001).

Table 180. 2,4-Dichlorophenoxyacetic acid

Geometric mean and selected percentiles of urine concentrations (in µg/L) for the U.S. population aged 6 to 59 years, National Health and Nutrition Examination Survey, 1999-2000.

	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)						Sample size
		10th	25th	50th	75th	90th	95th	
Total, age 6-59	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	1977
Age group								
6-11 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	1.30 (<LOD-1.90)	477
12-19 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	1.00 (<LOD-1.60)	677
20-59 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	823
Gender								
Males	*	< LOD	< LOD	< LOD	< LOD	< LOD	1.10 (<LOD-1.40)	962
Females	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	1015
Race/ethnicity								
Mexican Americans	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	695
Non-Hispanic blacks	*	< LOD	< LOD	< LOD	< LOD	< LOD	1.20 (<LOD-1.60)	520
Non-Hispanic whites	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	588

< LOD means less than the limit of detection, which averaged .09 µg/L (SD .29, maximum value 0.95).

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

Table 181. 2,4- Dichlorophenoxyacetic acid (creatinine adjusted)

Geometric mean and selected percentiles of urine concentrations (in µg/gram of creatinine) for the U.S. population aged 6 to 59 years, National Health and Nutrition Examination Survey, 1999-2000.

	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)						Sample size
		10th	25th	50th	75th	90th	95th	
Total, age 6-59	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	1977
Age group								
6-11 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	1.32 (.784-2.38)	477
12-19 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	.570 (.340-1.05)	677
20-59 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	823
Gender								
Males	*	< LOD	< LOD	< LOD	< LOD	< LOD	.667 (.476-.866)	962
Females	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	1015
Race/ethnicity								
Mexican Americans	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	695
Non-Hispanic blacks	*	< LOD	< LOD	< LOD	< LOD	< LOD	.570 (.420-1.05)	520
Non-Hispanic whites	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	588

< LOD means less than the limit of detection (see previous table).

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

2,4-Dichlorophenol

CAS No. 120-83-2

The chemical 2,4-dichlorophenol is a minor metabolite of 2,4-dichlorophenoxyacetic acid. It can also result from the metabolism of several other chemicals, or it may be a byproduct in the manufacture of chemicals. Median levels of 2,4-dichlorophenol were three times lower than levels measured in a non-random subsample from NHANES III (1988-1994) (Hill et al., 1995). 2,4-dichlorophenol levels in municipal waste-incinerator workers were three times higher than levels in the adults documented in this *Report* (Angerer, 1992).

Geometric mean blood levels of the demographic groups were compared after adjustment for the covariates of race/ethnicity, age, gender, and urinary creatinine. Children aged 6-11 years had levels slightly higher than the levels in people in the other two age groups. Non-Hispanic whites had a lower adjusted geometric mean 2,4-dichlorophenol level in urine than either Non-Hispanic blacks or Mexican Americans.

Table 182. 2,4-Dichlorophenol

Geometric mean and selected percentiles of urine concentrations (in µg/L) for the U.S. population aged 6 to 59 years, National Health and Nutrition Examination Survey, 1999-2000.

	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)						Sample size
		10th	25th	50th	75th	90th	95th	
Total, age 6-59	1.11 (.883-1.40)	< LOD	< LOD	.750 (.600-1.00)	2.90 (1.80-4.70)	11.0 (6.40-17.0)	22.0 (17.0-31.0)	1990
Age group								
6-11 years	1.27 (.878-1.83)	< LOD	< LOD	.820 (.560-1.40)	3.30 (1.50-7.70)	17.0 (6.50-27.0)	29.0 (17.0-83.0)	481
12-19 years	1.30 (.987-1.71)	< LOD	.400 (<LOD-.480)	.950 (.710-1.30)	3.50 (2.20-5.20)	11.0 (6.00-18.0)	21.6 (12.0-36.0)	679
20-59 years	1.05 (.838-1.32)	< LOD	< LOD	.700 (.560-.940)	2.50 (1.50-4.50)	9.40 (6.00-17.0)	21.0 (15.0-31.0)	830
Gender								
Males	1.35 (1.01-1.80)	< LOD	.360 (<LOD-.470)	1.00 (.680-1.50)	3.80 (2.12-6.30)	12.0 (6.40-18.0)	21.0 (14.0-31.0)	971
Females	.920 (.719-1.18)	< LOD	< LOD	.590 (.470-.800)	2.20 (1.20-3.60)	8.30 (4.70-18.0)	25.0 (11.0-32.0)	1019
Race/ethnicity								
Mexican Americans	1.80 (1.31-2.48)	< LOD	.430 (<LOD-.670)	1.00 (.770-1.60)	5.90 (3.90-8.80)	23.0 (14.0-34.0)	50.0 (28.0-78.0)	695
Non-Hispanic blacks	2.24 (1.48-3.39)	< LOD	.530 (.450-.690)	1.60 (.850-2.61)	8.80 (3.20-18.0)	22.0 (16.0-43.0)	39.0 (18.0-140)	518
Non-Hispanic whites	.892 (.701-1.14)	< LOD	< LOD	.600 (.450-.810)	2.00 (1.30-3.50)	7.20 (4.20-13.0)	17.0 (8.40-27.0)	602

< LOD means less than the limit of detection, which is 0.3 µg/L.

Table 183. 2,4-Dichlorophenol (creatinine adjusted)

Geometric mean and selected percentiles of urine concentrations (in µg/gram of creatinine) for the U.S. population aged 6 to 59 years, National Health and Nutrition Examination Survey, 1999-2000.

	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)						Sample size
		10th	25th	50th	75th	90th	95th	
Total, age 6-59	.994 (.807-1.22)	< LOD	< LOD	.794 (.605-.971)	2.15 (1.43-3.33)	6.79 (5.09-9.67)	13.9 (10.3-23.0)	1990
Age group								
6-11 years	1.37 (.974-1.92)	< LOD	< LOD	.966 (.604-1.36)	3.15 (1.49-7.63)	12.8 (6.79-23.7)	25.3 (12.8-76.9)	481
12-19 years	.877 (.694-1.11)	< LOD	.306 (.267-.341)	.645 (.494-.971)	2.19 (1.33-3.55)	5.70 (4.22-9.89)	10.3 (6.34-15.3)	679
20-59 years	.967 (.787-1.19)	< LOD	< LOD	.795 (.621-.962)	1.95 (1.32-3.06)	6.36 (4.62-8.84)	11.6 (8.70-21.8)	830
Gender								
Males	1.04 (.796-1.35)	< LOD	.337 (.274-.462)	.819 (.590-1.09)	2.51 (1.48-4.26)	7.55 (5.14-11.0)	12.3 (9.77-27.4)	971
Females	.955 (.771-1.18)	< LOD	< LOD	.735 (.582-.893)	1.91 (1.27-2.88)	6.66 (4.12-10.2)	15.3 (8.84-24.1)	1019
Race/ethnicity								
Mexican Americans	1.62 (1.20-2.19)	< LOD	.471 (.328-.657)	1.15 (.843-1.70)	4.00 (2.63-6.34)	19.8 (10.8-44.9)	48.7 (26.7-65.9)	695
Non-Hispanic blacks	1.52 (1.03-2.26)	< LOD	.419 (.330-.543)	1.16 (.672-1.97)	5.12 (2.38-7.20)	12.7 (6.36-41.7)	28.9 (8.47-161)	518
Non-Hispanic whites	.843 (.675-1.05)	< LOD	< LOD	.663 (.542-.870)	1.58 (1.18-2.35)	5.00 (3.27-8.70)	10.7 (6.43-19.2)	602

< LOD means less than the limit of detection (see previous table).

Atrazine mercapturate

Metabolite of atrazine (CAS No. 1912-24-9)

Atrazine is an herbicide that inhibits photosynthesis in broadleaf and some grassy weeds. It can be used in agriculture on a wide variety of crops, but of the 75 million pounds produced annually, 96% is used on corn and sorghum. Atrazine is degraded in the environment to several products and metabolized in people along multiple pathways. In animal studies, the hydroxy-atrazine class of degradation products and metabolites may produce kidney injury. Atrazine has low acute toxicity. Chronic exposure in animal studies has demonstrated reproductive and developmental effects. Amphibians may be particularly sensitive to environmental contamination. Human exposure to atrazine or its degradation products can occur through agricultural runoff into drinking-water systems. Workers can be exposed during residential and agricultural application of the herbicide. Children may be exposed by playing on lawns were atrazine was applied.

In people, atrazine is metabolized predominantly to its mercapturate. Atrazine mercapturate was detected in 3.3% of the NHANES 1999-2000 subsample. The low frequency of detection for atrazine mercapturate in urine was previously reported in the U.S. population (MacIntosh et al., 1999).

In one 1997 study of Minnesota children aged 3-13 years, urinary atrazine mercapturate levels averaged 0.55 µg/L (Adgate et al., 2001).

Table 184. Atrazine mercapturate

Geometric mean and selected percentiles of urine concentrations (in µg/L) for the U.S. population aged 6 to 59 years, National Health and Nutrition Examination Survey, 1999-2000.

	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)						Sample size
		10th	25th	50th	75th	90th	95th	
Total, age 6-59	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	1878
Age group								
6-11 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	449
12-19 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	639
20-59 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	790
Gender								
Males	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	919
Females	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	959
Race/ethnicity								
Mexican Americans	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	667
Non-Hispanic blacks	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	498
Non-Hispanic whites	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	549

< LOD means less than the limit of detection, which averaged 0.047 µg/L (SD 0.25, maximum value 0.79).

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

Table 185. Atrazine mercapturate (creatinine adjusted)

Geometric mean and selected percentiles of urine concentrations (in µg/gram of creatinine) for the U.S. population aged 6 to 59 years, National Health and Nutrition Examination Survey, 1999-2000.

	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)						Sample size
		10th	25th	50th	75th	90th	95th	
Total, age 6-59	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	1878
Age group								
6-11 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	449
12-19 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	639
20-59 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	790
Gender								
Males	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	919
Females	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	959
Race/ethnicity								
Mexican Americans	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	667
Non-Hispanic blacks	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	498
Non-Hispanic whites	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	549

< LOD means less than the limit of detection (see previous table).

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

Alachlor mercapturate

Metabolite of alachlor (CAS No. 15972-60-8)

Table 186. Alachlor mercapturate

Geometric mean and selected percentiles of urine concentrations (in µg/L) for the U.S. population aged 6 to 59 years, National Health and Nutrition Examination Survey, 1999-2000.

	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)						Sample size
		10th	25th	50th	75th	90th	95th	
Total, age 6-59	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	1942
Age group								
6-11 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	463
12-19 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	662
20-59 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	817
Gender								
Males	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	950
Females	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	992
Race/ethnicity								
Mexican Americans	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	679
Non-Hispanic blacks	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	507
Non-Hispanic whites	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	585

< LOD means less than the limit of detection, which averaged 0.09 µg/L (SD 0.36, maximum value 1.18).

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

Table 187. Alachlor Mercapturate (creatinine adjusted)

Geometric mean and selected percentiles of urine concentrations (in µg/gram of creatinine) for the U.S. population aged 6 to 59 years, National Health and Nutrition Examination Survey, 1999-2000.

	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)						Sample size
		10th	25th	50th	75th	90th	95th	
Total, age 6-59	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	1942
Age group								
6-11 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	463
12-19 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	662
20-59 years	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	817
Gender								
Males	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	950
Females	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	992
Race/ethnicity								
Mexican Americans	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	679
Non-Hispanic blacks	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	507
Non-Hispanic whites	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	585

< LOD means less than the limit of detection (see previous table).

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.